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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 08/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,088	VROUENRAETS ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-18* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-10 and 12-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Vrpiemraets et al.

Response to the Amendment

The Amendment filed on 06/6/2006 in response to the previous Non-Final Office Action (12/8/2005) is acknowledged and has been entered.

Claims 1-3 and 5-18 are currently pending.

Claim 11 is withdrawn from consideration as being drawn to a separately patentable invention from the claims previously under review.

Claims 1-3, 5-10 and 12-18 are currently pending.

Rejections Maintained:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 3-4 remain rejected and claims 5-6, 13-15 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Latouche et al. (Tetrahedron Letters 1995; 36: 1664-1666, IDS) in combination with Mauclaire et al. (US Patent 5,268,371, 1993).

Latouche et al. disclose a porphyrin derivative lacking an antibody which appears to 100% identical to the instantly claimed ring structure of formula (VIII), wherein the ring is a porphyrin ring having four aromatic phenyl substituted Ar's carrying one or more hydroxyl groups suitably linked via a ether linkage to a carboxyl group, e.g., COOH (compound shown on page 1665). The reference further teaches (page 1665, 1st paragraph, lines 3-5) that radiolabelled metalloporphyrins have significantly improved the efficacy of porphyrins for tumor detection, wherein the method can be improved by associating a radioactive metal complex and an antibody in order to deliver the reagent to a specific target. Moreover, Latouche et al. teach that the specific insertion of the metal in the porphyrin even in the presence of a good copper chelator like bovine albumin allows preliminary coupling of these ortho substituted porphyrins with antibodies before ^{64}Cu insertion (page 1666, lines 13-15).

Latouche et al. does not explicitly teach that the porphyrin derivative having four aromatic phenyl substituted Ar's carrying one or more hydroxyl groups is in turn linked via the COOH group to an antibody directed against a cell surface antigen of cancer or other diseased cells.

Mauclaire et al. teach derivatives of porphyrins and metalloporphyrins conjugated to a biologically active molecule (Title). With regards to the biologically active molecule, the patent teaches (column 8, lines 66-68 and column 9, lines 33-34) that such biologically active molecules include, but are limited to, antibodies, wherein the antibodies are directed against a cell surface antigen of the cancer cells. Specifically, Mauclaire et al. teach (column 5, lines 38-53) that the presence of the COOH group on the porphyrin gives them the property of being covalently bondable to biologically active molecules such as antibodies.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Latouche et al. and Mauclaire et al.. One would have been motivated to do so because as taught by both Latouche et al. and Mauclaire et al., porphyrin derivatives coupled to a biologically active molecule have a better affinity due to the presence of said biologically active molecule, e.g. target cell specificity (page 1665, 1st paragraph, lines 3-5 and column 9, lines 28-34 respectively). Thus, one of ordinary skill in the art would have a reasonable expectation that by conjugating an antibody with a porphyrin derivative as taught by Latouche et al. in view of Mauclaire et al., one would achieve a cancer cell specific porphyrin antibody conjugate which may be used for detection and/or treatment of tumor cells.

In response to this rejection, Applicants assert that that the present inventors were the first to effectively couple a monoclonal antibody to a porphyrin, to produce a conjugate which is optimal with respect to stability, binding affinity and photochemical properties, and which was capable of selective tumor targeting in vivo, wherein the inventors carefully controlled the conjugation conditions and employed a carboxymethylene linker moiety activated by a trifluorophenyl (TFP) group. Applicants further contend that although Latouche proposes to couple porphyrins with antibodies, this is not actually carried out or reported by Latouche. Moreover, Applicants contend that it is clear from the last sentence on page 1666 that linking had not actually been achieved by Latouche. As such, one of ordinary skill in the art would not have been motivated to arrive at the invention. Furthermore, Applicant's assert that Mauclaire does not cure the deficiencies of Latouche because there would not have been motivation to combine this disclosure with Latouche

since a person of ordinary skill would have had no expectation of success. In addition, Applicants assert Mauclaire relates to hydrosoluble porphyrin derivatives, and discusses coupling biologically active molecules including Mabs by alternative routes, although not involving TFP esters. For example, Applicants assert that Example 20 of Mauclaire describes the coupling of a porphyrin to an anti-ACE monoclonal antibody, wherein the monoclonal antibody is directly linked to the phenyl ring, without the intermediary of a carboxymethylene group. Also, Applicants submit that the immunoreactivity of the complex produced in Example 20 of Mauclaire is equal to 45% and there are 10 porphyrins per antibody (Example 20, last sentence). In contrast, Applicants contend that the immunoreactivity of the conjugates of the present invention was 93%, and further, that the present invention is drawn to "not more than four porphyrin molecules coupled to the monoclonal antibody (page 22, beginning of second paragraph). Lastly, Applicants submit that Mauclaire did not show that the conjugates produced are suitable for selective targeting and photodynamic therapy in vivo.

These arguments have been carefully considered, but are not found persuasive.
In response to Applicants assertion that the present inventors were the first to effectively couple a monoclonal antibody to a porphyrin group via an activated trifluorophenyl carboyxmethylene linker, the Examiner acknowledges that Applicants believe that they were the first to employ an activated trifluorophenyl carboxymethylene linker for the generation of an antibody-porphyrin conjugate. However, the Examiner recognizes that the claims are drawn to a product and not a process of producing the claimed compounds. Assuming, *arguendo*, that the claims were drawn to a produce by process, the Examiner recognizes that "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Regarding Applicants assertion that there is not motivation or suggestion to combine the two references, the Examiner recognizes that that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references In re Nomiya, 184 USPQ 607 (CPA 1975). However, there is no requirement that an "express, written motivation to combine must appear in prior art references before a finding of obviousness." See

Ruiz v. A.B. Chance Co., 357 F.3d 1270, 1276, 69 USPQ2d 1686, 1690 (Fed. Cir. 2004). For example, motivation to combine prior art references may exist in the nature of the problem to be solved (Ruiz at 1276, 69 USPQZd at 1690) or the knowledge of one of ordinary skill in the ad (National Steel Car v. Canadian Pacific Railway Ltd., 357 F.3d 1319, 1338, 69 USPQZd 1641, 1656 (Fed. Cir. 2004)). References are evaluated by what they suggest to one versed in the ad, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969). In the instant case, both Latouche et al. and Mauclaire et al. teach, as described above, porphyrin derivatives, wherein Latouche suggests linking antibodies to the porphyrin derivates to improve target specificity, whereas Mauclaire conjugates porphyrin derivates to biologically active molecules such as antibodies and teach that the presence of the COOH group on the porphyrin gives them the property of being covalently bondable to biologically active molecules such as antibodies. Regarding Applicants contention that the immunoreactivity of the Mauclaire conjugates is lower, as well as the number of porphyrins per antibody are higher, than the present invention, the Examiner agrees with Applicants assertion that the immunoreactivity of Mauclaire conjugate is 45% and that there are 10 porphyrins per antibody. However, the Examiner recognizes that arguments that rely on a particular distinguishing features are not persuasive when those features are not recited in the claims. Narrow limitation contained in the specification cannot be inferred in the claims where the elements not set forth in the claims are linchpin of patentability. See In re Philips Industries, Inc. v. State Stove & Mfg. Co., 522 F.2d 1137, 186 USPQ 458 (CA6 1975), 237 PTJA A-12. While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See Ex parte Oetiker, 23 USPQ2d 1641 (BPAI, 1992). Applicant is reminded that the claims define the subject matter of his invention and that the specification cannot be relied upon to read limitations into the claims. Lastly, with respect to Applicants assertion that Mauclaire did not show any in vivo examples, the Examiner concedes that Mauclaire does not appear to show any in vivo examples. However, the Examiner recognizes the intended use of the compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A composition is a composition irrespective of what its intended use is. See In re Tuominen, 213 USPQ 89 (CCPA 1982).

Claims 1-3 remain rejected and claims 5-10, 12-13 and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonnet et al. (US Patent 4,992,257, 1991, IDS) in combination with Latouche et al. (Tetrahedron Letters 1995; 36: 1664-1666, IDS) and Mauclaire et al. (US Patent 5,268,371, 1993) in view of Westerman et al. (Int. J. Cancer 1998; 76: 842-850).

Bonnet et al. teach (column 8, lines 37-68) dihydro and tetra-hydro porphyrins (referred to as chlorins and bacteriochlorins respectively, column 6, lines 21-24) having four aromatic phenyl substituted rings carrying one or more hydroxyl groups, wherein the hydroxyl groups may be in the ortho, para or meta position. With regards to the dihydro and tetra-hydro porphyrins, the patent teaches that the dihydro and tetra-hyrdro porphyrins include, but are not limited to, p-THPC, m-THPC, o-THPC and m-THPBC (column 6, Table 2). Bonnet et al. further teach (column 1, line 65 to column 2, line 1) that the compounds can be used as a form of cancer therapy, wherein the compound is administered to locate in the tumor followed by illumination of the tumor with light of a wavelength absorbed by the compound.

Bonnet et al. do not explicitly teach that the dihydro and tetra-hydro porphyrins (referred to as chlorines and bacteriochlorins respectively, column 6, lines 21-24) having four aromatic phenyl substituted rings carrying one or more hydroxyl groups are in turn linked to an antibody against a cell surface antigen of cancer cells. Nor does Bonnet et al. teach that the antibody and porphyrin derivatives are linked via an ether linkage through a COOH group.

The combination of Latouche et al. and Mauclaire et al. teach, as applied to claims 1 and 3-4 above, a porphyrin derivative having four aromatic phenyl substituted Ar's carrying one or more hydroxyl groups linked via a ether carboxyl group, e.g., COOH, to an antibody which binds a surface cell cancer antigen. Moreover, Mauclaire et al. teach (column 5, lines 38-53) that the presence of the COOH group on the porphyrin gives them the property of being covalently bondable to biologically active molecules such as antibodies, while Latouche et al. teach a method of generating the porphyrin derivative having an ether linked COOH group via alkylation of the phenolic hydroxyl by ethyl bromoacetate followed by saponification of the ester group (page 1665, last paragraph).

Westermann et al. teach (page 842, 2nd column, 1st full paragraph) that the major disadvantages of m-THPC phototherapy include, but are limited to, a relatively low tumor selectivity which, in view of the strong photoxic properties, can lead to undesired side effects in adjacent

normal tissues. As a way to circumvent this disadvantage, the reference teaches a conjugate comprising the photosensitizer metal-tetrahydroxyphenylchlorin (m-THPC) conjugated to polyethylene glycol which preserves its function of phototherapy and represents an interesting first step in favor of the strategy of conjugating photosensitizing dyes to anti-tumor antibodies (page 849, 2nd column, 2nd paragraph).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to specifically target a cancer cell with m-THPC. One would have been motivated to do so because as taught by Westerman et al., one of the major disadvantages with m-THPC phototherapy is the lower tumor selectivity that leads to undesirable side effects. Thus, one of ordinary skill in the art would have a reasonable expectation that by alkylating the hydroxyl groups of m-THPC followed by saponification in view of Latouche et al., one would achieve a covalently bondable COOH group on m-THPC which can be linked to an antibody for specific tumor localization of m-THPC.

Moreover, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker, 702 F.2d 989, 994-95, 217 USPQ 1, 5-6 (Fed. Cir. 1983).

In response to this rejection, Applicants submit that Bonnett discloses the synthesis of dihydroporphyrins, but makes no mention of or suggestion of the use of monoclonal antibodies. Applicants further submit that Mauclaire is not relevant for the reasons discussed above, and Westermann does not disclose or suggest coupling monoclonal antibodies to porphyrins having a polyethylene glycol group. Moreover, Applicants assert that while Westermann indicates that this observation represents "an interesting first step in favor of the strategy of conjugating photosensitizing dyes to anti-tumor antibodies, this is not a disclosure which would lead one of ordinary skill to the present invention based on the cited art combination. As further evidence of non-obviousness, Applicants note that around the time the present patent application was filed, problems were associated with coupling of photosensitizers to monoclonal antibodies. Applicants submit that the problems are as follows: (1) mTHPC lacks functional moieties for coupling to MAbs (mTHPC is hydrophilic (not water soluble), which does not allow well-controlled conjugateion to

hydrophilic MAb molecules); (2) Impairment of MAb integrity, immunoreactivity and pharmacokinetic behavior can occur upon coupling of mTHPC, due to, e.g., uncontrolled conjugation procedures and photochemical damage; and (4) Impairment of photodynamic properties of mTHPC, can occur, resulting in impaired therapeutic (PDT) effects. Regarding these 4 problems, Applicants submit that they have overcome problem (1) by tetracarboxymethylating mTHPC and esterifying the four carboxylic groups with TFP (see Figure 1), overcome problem (2) by controlled hydrolysis and isolation of mTHPC-TFP mono-esters (see Figure 1), overcome problem (3) by conjugating the antibody and mTHPC in the dark and under a N2 atmosphere, and overcome problem (4) by in in vitro PDT experiments showing that mTHPC retained photochemical properties (page 19, last paragraph to page 20 and Figures 6A and 6B). In summary, Applicants submit that it is clear that one of ordinary skill would not have been motivated to arrive at the presently claimed invention based on the combined disclosures relied on by the Examiner.

These arguments have been carefully considered, but are not found persuasive.

With regards to Applicants arguments pertaining to the cited combination, it must be remembered that the references are relied upon in combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references, which make up the state of the art with regard to the claimed invention. Furthermore, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In this case, the cited references teach the following: (1) Bonnet et al. teach dihydro and tetra-hyrdro porphyrins including, but are not limited to, p-THPC, m-THPC, o-THPC and m-THPBC which can be used in photodynamic cancer therapy (column 6, Table 2); (2) Westerman teach that the major disadvantages of m-THPC phototherapy include, but are limited to, a relatively low tumor selectivity which, in view of the strong phototoxic properties, can lead to undesired side effects in adjacent normal tissues; (3) Mauclaire conjugates porphyrin derivates to biologically active molecules such as antibodies and teaches that the presence of the COOH group on the porphyrin gives them the property of being covalently bondable to biologically active molecules such as antibodies; and (4) Latouche et al. teach a method of generating the porphyrin

derivative having an ether linked COOH group via alkylation of the phenolic hydroxyl by ethyl bromoacetate followed by saponification of the ester group. As such, one of skill in the art would have a reasonable expectation of success that by generating a mTHPC antibody conjugate, one would achieve a covalently bondable COOH group on m-THPC which can be linked to an antibody for specific tumor localization of m-THPC. With respect to Applicants further evidence of non-obviousness, the Examiner recognizes that the arguments of counsel cannot take the place of evidence in the record. In re Schulze,346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. As such, claims 1-3 remain rejected and claims 5-10, 12-13 and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonnet et al. (US Patent 4,992,257, 1991, IDS) in combination with Latouche et al. (Tetrahedron Letters 1995; 36: 1664-1666, IDS) and Mauclaire et al. (US Patent 5,268,371, 1993) in view of Westerman et al. (Int. J. Cancer 1998; 76: 842-850).

New Rejection Necessitated by Amendment:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 5 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Mauclaire et al. (US Patent 5,268,371, 1993).

Mauclaire et al. teach derivatives of porphyrins and metalloporphyrins derivative carrying four aromatic substituents each of which carries at least one hydroxyl group which is conjugated to a biologically active molecule via a CH_2COOH linking group (Title and Example 8). With regards to the biologically active molecule, the patent teaches (column 8, lines 66-68 and column 9, lines 33-34) that such biologically active molecules include, but are limited to, antibodies, wherein the antibodies are directed against a cell surface antigen of the cancer cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mauclaire et al. (US Patent 5,268,371, 1993) in further view of Bendig et al. (WO 92/15683, 1992).

Mauclaire et al. teach, as applied to claims 1, 3, 5 and 18 above, derivatives of porphyrins and metalloporphyrins derivative carrying four aromatic substituents each of which carries at least one hydroxyl group which is conjugated to a biologically active molecule via a CH_2COOH linking group (Title and Example 8). With regards to the biologically active molecule, the patent teaches (column 8, lines 66-68 and column 9, lines 33-34) that such biologically active molecules include, but are limited to, antibodies, wherein the antibodies are directed against a cell surface antigen of the cancer cells. Moreover, the patent teaches that the porphyrin derivatives may be used as diagnostic or therapeutic agents for tumors.

Mauclaire et al. do not explicitly teach that the antibody is mMAb 425.

Bendig et al. teach that murine monoclonal antibody 425 (Mab 425) binds to a polypeptide epitope on the external domain of the human epidermal growth factor receptor and inhibits the binding of epidermal growth factor at both low and high affinity EGFR sites (page 3, lines 7-12). Moreover, Bendig et al. teach that enhanced expression of EGFR is found to occur on malignant tissues from a variety of sources, thus making mAb 425 a useful agent for the diagnosis and therapeutic treatment of human tumors (page 3, lines 12-21).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to conjugate mAb 425 to the porphyrin derivatives taught by Mauclaire et al. in view of Bendig's teachings that mAb 425 is a useful agent for the diagnosis and treatment of human tumors due to EGFR's enhanced expression in a variety of tumors. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by conjugating mAb 425 to the

porphyrin derivatives, one would achieve a porphyrin:mAb 425 immunoconjugate useful for the treatment or diagnosis of tumors characterized by enhanced EGFR expression.

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Therefore, NO claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER